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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,923	05/14/2007	Manpreet S. Wadhwa	PC027698A	4848

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EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,923	WADHWA ET AL.	
	Examiner	Art Unit	
	FOZIA M. HAMUD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-15* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Claims:

1. Claims 1-15 are pending and under consideration.

***Petition under* 37 C.F.R§1.47(a)**

2. The petition filed under 37 C.F.R§1.47(a) to accept the application without the signature of joint inventor Manpreet Wadhwa, who refused to sign the Applicaiton has been granted.

Claim Objection:

3. Claim 1 is objected to because of the following informalities: The term “excipient” in line 4 should be amended to recite “excipients". Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 7, 11-15 are rejected under 35 U.S.C. 112, first paragraph, while being enabling for a formulation comprising growth hormone in an aqueous solution, a buffer that maintains the pH of the formulation from about 5 to 7, a non-ionic surfactant and up to 1% of polymer stabilizer, is not enabling for a formulation comprising growth hormone in an aqueous solution, a buffer that maintains the pH of the formulation from about 5 to 7, a non-ionic surfactant and up to 70% or 20% of polymer stabilizer as recited in claims 7 and 11, respectively. The specification does not enable any person skilled in the art

to which it pertains, or with which it is most nearly connected, how to make or use the invention commensurate in scope with these claims.

Claims 7 and 11-15 encompass a formulation comprising growth hormone in an aqueous solution, a buffer that maintains the pH of the formulation from about 5 to 7, a non-ionic surfactant and up to 20% or 70% of polymer stabilizer, however, the specification teaches that the polymer stabilizer used is 1% PEG 20,000 or 3350, (see table VIII on page 22). The specification fails to teach whether the claimed formulation is stable in such high concentration of a polymer stabilizer. Furthermore, the relevant art does not teach the use of such high polymer stabilizer. For example Feng et al, (Biotechnology Techniques, April 1998, Vol.12, No.4, pages 289-293) teaches that the optimum concentration of PEG to improve recovery of recombinant protein is 1% and that increasing PEG to 3% or 4% decreased recovery or purification of the protein of interest, (see page 290, column 2). In the instant case, the specification does not provide adequate guidance as to the effect that such a high concentration of polymer would have the stability, recovery and activity of the growth hormone.

The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant case, the lack of

direction/guidance presented in the specification regarding the effect 20% or 70% concentration of a polymer stabilizer on the stability, recovery and activity of growth hormone, the absence of working examples directed to same, the relevant art which teaches that the optimum concentration of PEG is 1% and slight increase to 3% or 4% resulted in decrease in recovery, the specification fails to provide an enabling disclosure for a formulation comprising growth hormone in an aqueous solution, a buffer that maintains the pH of the formulation from about 5 to 7, a non-ionic surfactant and up to 70% or 20% of polymer stabilizer.

Rejections Under § 112, second paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5a. Claim 1, line 3 and claim 10, line 5, recite the phrase "optionally further comprising", which renders the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention.

5b. Claim 2 recites the limitation "human growth hormone" in line 1, however, claim 1 (from which it depends) only recites "growth hormone". Thus, there is insufficient antecedent basis for this limitation in the claim.

5c. Claim 13 recites the acronym “hGH". However, there is insufficient antecedent basis for this limitation in the claim, because claim 11 from which claim 13 depends does not recite this acronym.

5d. Claim 15 recites “after storage for 12 months…”, however, there is insufficient antecedent basis for this limitation in the claim, because claim 14, (from which claim 15 depends) does not recite anything about “storage”. Claim 14 just recites that the formulation is stable.

Claims 2-10 and 12-15 are also rejected under 35 U.S.C. 112, second paragraph in so far as they depend on claims 1 and 11 for the limitations set forth above.

Priority:

5. Based on the information given by Applicants and an inspection of the patent applications, the Examiner has concluded that the subject matter defined in claims 1-15 of this application is supported by the disclosure in U.S. Provisional Application 60/531,843, filed on 23 December 2003. Accordingly, 23 December 2003 is used for the purposes of applying prior art.

Claim rejections-35 USC § 102:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6a. Claim 1-6, 9-10 are rejected under 35 U.S.C § 102(b) as being anticipated by WO97/29767, (McNamara et al published on 21 August 1997).

Because of the "optionally further comprising" language in claim 1, the Examiner has interpreted that the limitations after this phrase are "optional" and therefore not necessarily required for the invention.

The instant claim 1 is drawn to a formulation comprising a growth hormone, (0.1 mg/ml up to 20 mg/ml), in an aqueous solution, a buffer that maintains the pH of about 5-7, a non-ionic surfactant and a polymer stabilizer, claims 2-6 and 8-10 further limit non-ionic surfactant, polymer or buffer and also recite specific concentrations or percentages.

McMAMARA et al disclose liquid formulations comprising recombinant human growth hormone (0.1 mg/ml up to 20 mg/ml), citrate buffer, non ionic surfactant and the excipient polyethylene glycol, wherein the pH of the formulation is from about 5-7.5, (see page 7, lines 16-27, page 8, lines 5-30, page 17, table 4 and pages 20-21).

Although the McNAMARA et al reference does not explicitly teach that their formulation is stable after at least one freezing and subsequent thawing event, the formulation taught by McNamara et al would be inherently stable after at least one freezing and subsequent thawing event, because it comprises a buffer that maintains the pH from about 5 to 7, the non-ionic surfactant and a polymer stabilizer as required by claim 1 of the instant application.

Therefore, McMAMARA et al reference anticipates instant claims 1-6 and 9-10 in the absence of any evidence to the contrary (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)).

6b. Claims 1-6 are rejected under 35 U.S.C § 102(b) as being anticipated by

US20020077461, (BJORN et al published on 20 June 2002).

Because of the "optionally further comprising" language in claim 1, the Examiner has interpreted that the limitations after this phrase are "optional" and therefore not necessarily required for the invention.

The instant claim 1 is drawn to a formulation comprising a growth hormone in an aqueous solution, a buffer that maintains the pH of about 5-7, a non-ionic surfactant, a polymer, (freeze/thaw) and claims 2-6 further limit the growth hormone as being a recombinant, non-ionic surfactant, polymer or buffer and also recite specific concentrations and percentages.

BJORN et al disclose aqueous formulations comprising a human growth hormone, histidine buffer, non ionic detergent, (polysorbate 20) and the excipient polyethylene glycol, (see sections 0057, 0069, 0072, 0074, 0079 and claims). Although the BJORN et al reference does not explicitly teach that their formulation is stable after at least one freezing and subsequent thawing event, the formulation taught by BJORN et al would be inherently stable after at least one freezing and subsequent thawing event, because it comprises a buffer that maintains the pH from about 5 to 7, non-ionic surfactant and a polymer stabilizer as required by claim 1 of the instant application.

Therefore, BJORN et al reference anticipates instant claims 1-6 in the absence of any evidence to the contrary (*In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)).

Conclusion:

7. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjuanth N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fozia Hamud
Patent Examiner
Art Unit 1647
05 November 2008

/Bridget E Bunner/
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